Sex-based differences in patients with community-acquired bacterial meningitis: a prospective nationwide cohort study

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Background: Sex-based issues have been increasingly recognised in infectious diseases, influencing susceptibility to pathogens, immune response to illness, disease course and response to treatment. We investigated differences in clinical features, management and outcome of adult men and women with community-acquired bacterial meningitis.

Material/methods: From 2006-2014, adults with community-acquired bacterial meningitis were prospectively evaluated in a nationwide cohort study in the Netherlands. Parametric and nonparametric tests were used to compare characteristics between men and women, and sex was investigated as a predictor of outcome using logistic regression.

Results: We evaluated 1440 episodes of meningitis; 50% were males. Females were older (median age 62 vs 60 years, p=0.002) and presented more frequently with otitis/sinusitis (270 of 712 [38%] vs 219 of 718 [30%], p=0.003) and neck stiffness (533 of 685 [78%] vs 461 of 662 [70%), p=0.001) and less frequently with focal neurological deficits (174 of 716 [24%] vs 208 of 715 [29%), p=0.04) as compared with males. Men more frequently had remote head injury (42 of 679 [6.2%] vs 14 of 673 [2.1%, p<0.001) and immunocompromise (214 of 720 [30] vs 159 of 720 [22%, p=0.001), including alcoholism (63 of 662 [9.5] vs 24 of 675 [3.6%), p<0.001), as compared with women. Pathogen distribution among sexes differed, mainly driven by a high rate of listeria meningitis among men (50 of 720 [7%] vs 26 of 720 [4%, p=0.005). Females exhibited higher levels of inflammatory parameters (median C-reactive protein 211 [97-328] vs 170 [78-288], p<0.001; erythrocyte sedimentation rate 48 [28-75] vs 33 [17-66], p<0.001), and despite greater illness severity on admission (mean Dutch Meningitis Risk Score 28±12 vs 26±12, p=0.01), they were less likely to be admitted in an intensive care unit (adjusted OR 0.66, 95% CI 0.52-0.85; p=0.001) or receive mechanical ventilation (adjusted OR 0.52, 95% CI 0.36-0.74; p<0.001) than men. Male sex was an independent predictor of unfavourable outcome (adjusted OR 1.56, 95% CI 1.13-2.16; p=0.007), and while dexamethasone reduced the rate of adverse outcome in both sexes, this effect was more pronounced in women (75 of 147 [51%] to 175 of 556 [32%]; OR 0.44, 95% CI 0.30-0.64; p=0.001) than in men (85 of 170 [50%] to 190 of 537 [35%]; OR 0.55, 95% CI 0.39-0.78; p=0.001), although we did not observe a significant
interaction between sex and dexamethasone (p=0.40). Among survivors, cognitive impairment was more common in men (104 of 488 [21%] vs 77 of 509 [15%], p=0.01).

**Conclusions:** There are sex-based differences in patients with community-acquired bacterial meningitis. Male sex is an independent risk factor for adverse outcome, and a stronger pro-inflammatory response may render women more responsive to treatment with corticosteroids. These differences suggest a need for individualised management strategies that take sex-based factors into consideration.